



# Practical and Theoretical Barriers to the Prevention of Accelerated Atherosclerosis in Systemic Lupus Erythematosus

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## Commentary SLE

# Practical and theoretical barriers to the prevention of accelerated atherosclerosis in systemic lupus erythematosus

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## Abstract

Accelerated atherosclerotic vascular disease (ASVD) is a major cause of death in systemic lupus erythematosus (SLE). Although many authorities are calling for aggressive assessment and management of cardiac risk factors in patients with SLE, both theoretical and practical barriers to this approach exist. It seems that SLE and/or its treatment are themselves strong risk factors for the development of ASVD and it is unclear how much this risk can be decreased by the control of traditional risk factors. Studies from several centers have shown that suboptimal risk factor management and barriers to acceptance of these measures must also be studied further.

**Keywords:** atherosclerosis, cardiac risk factor, coronary artery disease, systemic lupus erythematosus

## Introduction

Aggressive and accelerated atherosclerosis is a major problem in systemic lupus erythematosus (SLE) and is one of its major causes of death, an observation first made more than 20 years ago by Urowitz [1]. Coronary artery disease develops in 6–9% of SLE patients and accounts for up to 36.4% of deaths in SLE. High rates of atherosclerotic vascular disease (ASVD) are particularly striking in young women with SLE, normally at low risk. The incidence of myocardial infarction in women with SLE aged 35–44 years is 50-fold greater than in women of similar ages from a population-based sample [2]. Non-invasive methods of demonstrating atherosclerotic disease, such as carotid duplex ultrasound, electron-beam computed tomography, and thallium perfusion scanning, and one autopsy study, suggest that symptomatic disease might be the tip of the iceberg. The true incidence could be as high as 74% [3–10].

The pathophysiology of SLE-associated atherosclerosis is unknown, but the emerging picture is that many of the

same risk factors as those observed in normal individuals are also involved. This has motivated authorities in both rheumatology and preventive cardiology to advocate more aggressive risk factor assessment and management of risk factors [11–17]. There are theoretical and practical barriers to improving atherosclerosis-related outcomes in SLE suggesting that this approach will be challenging, and the potential benefit is yet unknown.

First, when risk factors are examined quantitatively, SLE and/or its treatment (most probably with corticosteroids) are the most important risk factors. Indeed, data from Esdaile and colleagues suggest that even after adjusting for 'normal risk', SLE and/or its treatment increases the risk of coronary artery disease 5–10-fold [18]. This suggests that even if physicians were perfectly virtuous, sought out risk factors aggressively and followed guidelines scrupulously; and patients were tolerant, compliant, and responsive to lipid-lowering strategies and blood pressure control, for example, there would still be excess mortality and morbidity from ASVD.

Second, studies from Toronto and Baltimore show that risk factor identification and, by implication, treatment fall short of what one would predict from the importance of the problem [13,19]. We know that patients with chronic diseases such as SLE, rheumatoid arthritis, and diabetes are less likely to receive the highest quality of preventive health care, perhaps because more urgent problems must be dealt with first, or perhaps because of patients' and physicians' exhaustion in dealing with chronic health problems. Patients can find it difficult to change their lifestyles and take additional medications on top of complicated regimens or little reinforcement from their providers. In recruiting patients with SLE and hyperlipidemia for a statin dosing study, our experience has been that the patients who are the most willing to participate are relatively young and healthy, with very mild SLE, and few other health problems or medications. Among those patients with more long-standing and severe SLE, reasons for non-participation have included, 'I'm flaring and don't want to take another medication that might make me sick', 'I'm trying to get healthy', and 'I'm too sick and have too many doctor's appointments already'.

## Conclusion

HL Mencken once quipped, 'For every complex problem, there is a solution which is simple, neat and wrong'. We have known for over 20 years of the late complications of SLE. The received wisdom that we need only try harder to implement the known effective preventive strategies for normal individuals is simple and neat, but might be wrong or incomplete.

Several questions remain unanswered in our search for a successful approach to the prevention of ASVD in SLE. The etiologic factors responsible for vascular injury in SLE need to be understood more precisely. For example, do short-term hypertension, hyperlipidemia, and immune complex generation of an SLE flare do as much or more damage to the endothelium as does lower-grade inflammation or exposure to traditional risk factors for many years? In addition, a better understanding of patient social and cultural factors will be essential to achieving acceptance of lifestyle changes and medications. Progress will only be made as basic science brings an understanding of the mechanisms of accelerated atherosclerosis in SLE and as clinical studies address both the efficacy and the effectiveness of existing and improved risk factor control.

## Competing interests

None declared.

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